

## **REMARKS**

### **Status of the Claims**

Claims 1-10 are pending in the present application. Claim 1 is independent. Claims 2, 3 and 10 stand withdrawn, as being drawn to nonelected subject matter.

Claims 1, 4, 5 and 7-10 have been amended. Amendments to the claims are supported throughout the specification as filed. For example, support for the amendments can at least be found at page 5, lines 19-20; page 6, lines 1-2; and page 8, lines 17-18. Thus, no new matter has been added by way of amendment to the claims. Reconsideration of this application, as amended, is respectfully requested.

### **Request for Entry of Response after Final Rejection**

This response should be entered after final rejection because it believed to automatically place the application in condition for allowance.

In the event that the Examiner disagrees and finds that this response does not place this application into condition for allowance, the Examiner is requested to enter this response because it places the application into better condition for appeal.

### **Rejection under 35 U.S.C. § 112, first paragraph**

Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to meet the enablement requirement. This rejection is respectfully traversed.

It is asserted in the Office Action at page 4 that:

it is unpredictable if an HLA-E chimeric molecule that has the first portion of the  $\alpha 2$  domain, or the first portion of the  $\alpha 2$  domain and a part of the  $\alpha 1$  domain, replaced with the corresponding domain portion of HLA-G1 can be used for the disclosed purpose of cell surface expression and inhibition of NK cell activity in xenotransplantation.

In particular, it is alleged in the Office Action that Matsunami et al. (BBRC, 347 (2006) 692-697) demonstrates that when the  $\alpha 1$  domain of the HLA-E is replaced with that of HLA-G1, there is no expression of chimeric HLA-E molecule.

The Office Action refers to Table 11 of the Specification. However, there is no "Table 11" in the Specification. Applicants believe this is meant to be a reference to Table 1 found on page 11 of the Specification as filed.

It is alleged at page 4 of the Office Action that:

[w]hen the inventors replaced the latter part of  $\alpha 2$  domain with the corresponding part of HLA-G1 (also replaced the SP of HLA-G1 with the SP of HLA-E), or when they replaced the  $\alpha 1$  domain with the corresponding part of HLA-G1, cell surface expression was not increased over that seen with native HLA-E.

Applicants believe this allegation is meant to refer to Constructs 12 and 8 found in Table

1. Construct 12 in Table 1 replaced the SP domain and the latter part of the  $\alpha 2$  domain and cell surface expression with Construct 12 was increased over that seen with native HLA-E, as shown in Table 1. Further, Construct 8 replaced the SP domain, and the whole  $\alpha 1$  domain. Applicants respectfully disagree with the allegation that amended claim 1 is not enabled by the specification, as filed.

Thus, contrary to the allegations in the Office Action, increased cell surface expression was shown for Construct 12 in Table 1. Further, Construct 8 is not an embodiment recited in claim 1. Instead claim 1, element (3) recites “an HLA-E chimeric molecule replacing the signal peptide (SP) ... with a reformed SP... replacing a part of the  $\alpha 1$  domain including the serine corresponding to amino acid 11 of SEQ ID NO:2 and all or part of the  $\alpha 2$  domain of the HLA-E molecule.” As shown in Table 1, simply replacing the SP leads to some expression, while Example 8, which replaces both the SP and the  $\alpha 1$  domain, does not show expression. The other Tables describe replacing only amino acid 11 of the  $\alpha 1$  domain, the SP and amino acid 147 of the  $\alpha 2$  domain, and reducing cytotoxicity (see page 14, Table 3, Construct 5). Thus, Applicants respectfully submit that one of skill in the art would know how to make and use the claimed invention.

Applicants respectfully submit that the claims, as amended, comply with the enablement and written description requirements of 35 U.S.C. § 112, first paragraph. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

**Rejection under 35 U.S.C. § 112, second paragraph**

Claims 1 and 4-9 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

The Examiner has set forth certain instances wherein the claim is not clearly understood. The Examiner has suggested adding references to sequences defined by specific SEQ ID NOs and/or specific regions of disclosed sequences, including identifying SEQ ID NOs.

Applicants have amended claims 1, 4, 5 and 7-9 to reference specific sequences as suggested by the Examiner. Applicants respectfully submit that the claims, as amended, particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

### CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Stephanie A. Wardwell, PhD, Registration No. 48,025, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

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